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Biological Aspects of Laser Radiation

A Review of Hazards

U. S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
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BIOLOGICAL ASPECTS OF LASER RADIATION
A REVIEW OF HAZARDS

Wellington Moore, Jr., D.V.M., Ph.D.

Bureau of Radiological Health
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FOREWORD

The rapidly expanding technology in the laser field and the increased commercial and institutional applications of lasers makes it important that those responsible for protection of the public health and safety have the current information on the biological effects of radiation from lasers. This report reviews the scientific and technical literature available prior to 1968 on this subject and includes a discussion of both thermal and nonlinear effects. The report is intended as a reference for those concerned with the potential hazards of lasers and the establishment of programs for the prevention or control of exposure.

Raymond T. Moore

Raymond T. Moore, M.D.
Acting Bureau Director

INTRODUCTION

Lasers emit highly directional, spatially confined, beams of intense monochromatic radiation. This radiation is potentially harmful to man. Considerable effort has been spent in studying the biological effects of this type of radiation. Of the possible biological effects of laser radiation studied to date, the eye appears to be the most sensitive organ to injury. The lens of the eye focuses the incident visible laser radiation upon the retina resulting in an energy density at the retina of several orders of magnitude greater than the incident level at the cornea. For this reason, corneal intensities of visible laser radiation that could produce retinal damage are many orders of magnitude less than the incident intensities required to produce skin damage.

For radiation in the near-ultraviolet, near-infrared, and visible region of the spectrum, the retina is the critical part of the eye; for the ultraviolet and far-infrared regions, the portions of the eye anterior to the retina may be of greater concern. Already in the literature, there are substantiated case reports of severe ocular damage resulting from accidental exposure to laser radiation (1-3). Other aspects of personnel protection include protection against skin exposure, and protection from electrical shock.

The levels of laser radiation that constitute a hazard are difficult to establish because of variations in the type of laser and variations in biological factors. Since 1960 when T. H. Maiman (4) reported building the first ruby laser, a very large and diverse family of lasers has been developed. Laser radiation can be produced in a variety of generating modalities. Different wavelengths, intensity levels, pulse durations, and pulse repetition rates all influence directly the possibility of tissue damage. The array of devices utilizing the various properties makes it impractical to list each device. Biological factors applicable to all tissues, such as pigmentation, vascularity, and spectral absorption of the energy influence the degree of damage. In addition, there are organ-specific factors which influence the degree of damage to a particular organ. In the case of the eye, for example, pupil size, convergence power of the cornea and lens, and distance from the lens to retina, all influence the threshold level for damage. Because of the multiplicity of these factors it is unwise to establish one threshold value for biological damage for all types of laser systems and conditions of operation.

MODE OF ACTION

The action of laser radiation on biological tissues may be divided into two broad areas: (1) those attributed to heat; (2) those not attributed to heat (nonlinear effects). These nonlinear effects include mechanical effects such as target impulse, target recoil, pressure effects from thermal expansion with or without change of phase, and shock wave production; ionization effects and X-ray production; free radical formation and harmonic generation of other wavelengths in crystalline tissue components.

The production of nonlinear effects requires energy intensities that are catastrophic in biological tissues. If the impingement of a laser beam on matter is considered in a conventional manner, its effects have to be accounted for by the quanta released to the atoms and molecules through which it passes. Unlike X-ray quanta which are energetic enough to effect release of electrons from atoms to produce ions, the longer wavelength radiations are only sufficiently energetic to excite atoms by changing the orbital arrangement of electrons in the case of ultraviolet light, excite resonant molecules in the case of visible light, and vibrate atoms in the case of infrared light. The majority of these processes result in a rise in temperature although some may produce photochemical changes where the chemical systems are capable of being unbalanced by energy changes. Most of the laser lesions in biological systems are attributable to heat or known photochemical processes; however, there are some observations which cannot be explained entirely by these mechanisms. At high intensities common with some lasers, optical processes of absorption and a re-radiation may not be linear (5).

Thermal Effects

Laser-induced thermal lesions have been produced in various tissues in several animal species and in man. A theory that has been advanced to explain thermal injury includes: (1) thermal alteration of protein, (2) other possible alterations in metabolic processes, and (3) nonprotein induced alterations in physical characteristics of cells (6). In studies on the effects of ruby laser radiation on the retina, Vos (7) indicated that most of the energy is absorbed by the melanin granules of the pigment epithelium. This absorbed energy is converted into heat which is transferred by conduction, convection, and radiation to the proteins around them. If these proteins are sufficiently heated, they may be denatured or coagulated. More vigorous heating produces vaporization of the tissue water with consequent disruption of tissue by bubbles of steam.

Attempts have been made to measure retinal temperature in the rabbit with sensitive thermocouples (8-10). Resolution of temperature changes has been limited by the properties of the thermocouples. Najac et al. (9) reported the temperature rise varied from 12.5 to 20.6°C above normal for a retinal threshold burn (small amount of coagulation in the

center of the lesion) measured directly at the burn site. Mellerio (10, 11) found that just outside the area exposed to a laser beam of 5 millijoules (mJ) of energy, the retinal temperature rose from its normal 39°C to over 60°C. McGuff et al. (12) made temperature measurements with thermocouples implanted in tumors in the hamster. When the thermocouple was placed just beneath the mucosa covering the tumor, a temperature of 445°F was measured after a 140 J ruby laser pulse. At a depth of 2.5 mm below the tumor surface a temperature of 145°F was recorded. This pulse (140 J) was considerably above threshold.

Irradiation through the intact skull in small animals led to death after relatively small doses, 100-200 J (13). This was ascribed to super-heating tissue to a gaseous state in a closed cavity with the production of an explosive force which drove the brain to the base of the skull forcing it through the tentorium and foramen magnum with fatal results.

Irradiation of the skin produced lesions resembling thermal burns. The amount of damage varied with the intensity of the irradiation and the degree of pigmentation. Irradiation of porcine skin with an energy of 10 J (image diameter of 2 mm) produced subepidermal vesicles partially filled with fluid (14). Fine et al. (15, 16) irradiated the pigmented skin of the hamster and produced a lesion characterized by a small central area of penetrating injury resembling a second degree burn surrounded by an area of less intense damage that went on to vesiculate. On microscopic examination, a punched out, well-defined, and sharply demarcated area of destruction was noted which later became infiltrated with inflammatory cells and was ultimately replaced by fibrous scar tissue. Unlike the gradual transition from maximum damage to normal tissue as seen in a thermal burn, the laser-irradiated area was separated from nonirradiated areas by a rather sharp line of demarcation (17). The sharp demarcation of necrosis suggests that the brief period of impact was not sufficient to allow heat to transfer to adjacent tissue. Laser radiation at a level of approximately 30-50 J produces relatively little damage to the skin of hamsters, but variations in the severity of the injury suggest a relation to the amount of pigment or to the number of hair follicles in the area (15).

In man, skin with high pigmentation showed significant changes in the epidermis after impact of a low-energy laser (5-10 J), including superficial scaling, superficial charring, crusting, and even ulceration (18). No evidence of changes was noted in skin of low pigmentation at this energy level. With high energy densities up to 100 J, significant alterations may develop in low pigmented skin after a single impact, such as anesthetic areas with changes in the epidermis and significant modifications in the deeper blood vessels.

Morphologic and biochemical data indicate that the cytological effect of laser radiation depends upon the structural and absorption characteristics of the target tissue for the incident wavelength.

Highly pigmented, very cellular tissues with sparse supporting collagenous stroma may be instantaneously vaporized. Tissues with dense collagenous stromata may be non-functional but not disintegrated. Ham et al. (19) have reported that the absorption of radiation by pigmented retinal epithelium was minimal at 4,000 Å, maximal at 5,000 to 5,500 Å, and diminished to negligible values at 13,000 Å. The pigmented retinal epithelium absorbs approximately 70% of the light at 6,943 Å and only 20% at 10,600 Å (20).

Thorell and Chance (21) have shown that nonpigmented cells show greatest optical density at approximately 4,150 Å and do not absorb appreciably in the red wavelengths. Bessis and Ter-Pogossian (22) destroyed red blood cells with laser radiation but found white blood cells unaffected. By suitably staining the white cells they were able to destroy those parts which took up the stain. A variety of cell types grown in tissue culture have been irradiated (6,943 Å) and, in general, cells have been injured or destroyed in proportion to their degree of pigmentation (23, 24). Although nonpigmented cells did not appear to be damaged immediately after laser radiation, subtle changes were detected later. Rounds (23) observed cytoplasmic bleeding in unpigmented cells within 10 minutes after exposure to 0.125 J/cm² of 3,471 Å laser energy. Irradiation of transparent HeLa cells caused a decrease in oxygen consumption, and irradiation (2.5 J/cm²) of intact chick hearts slowed the contraction rate (24). Cells can be sensitized to light by various organic compounds including many dyes such as erythrosine, acriflavine and acridine orange. Rounds et al. (24) demonstrated that nonpigmented cells could be sensitized to laser injury by prior vital staining with dyes such as Janus green. Moreover, laser irradiation of unstained cells appeared to make them more sensitive to Janus green. Experimental evidence suggests that laser radiation produces cytologic effects if a suitable substance is present to absorb the laser energy at the emitted wavelength and that the effects depend on the amount of energy absorbed by the cells.

Nonlinear Effects

A good deal of effort has been directed toward defining the nonlinear effects of laser radiation and how they are mediated in biological systems. Considerable speculation and disagreement exist over the possible mechanisms involved. Some of the mechanisms which have been implicated in the nonlinear effects include: (1) mechanical effects including target impulse and target recoil, (2) pressure effects from thermal expansion with or without change of phase and shock wave production, (3) ionization effects and X-ray production (not likely in biological tissues), (4) free radical formation, (5) harmonic generation of other wavelengths.

The mechanical effects of laser radiation on materials has been discussed by Burkhalter (25) and he concludes that the total momentum of pulses from the most powerful lasers to date is of negligible magnitude (3,000 J of pulse energy per dyne-second of impulse). However,

there is considerable recoil of the target from the mass blown away at the surface. No results were available for biological tissue.

Fine et al. (26) indicated that pressure waves could be produced as follows: (1) volatilization of material from the surface with generation of a mechanical impulse into the biologic system, (2) transient heating and associated thermal expansion of volume, without change of phase, (3) transient heating with change of phase, especially to a gaseous phase.

Litwin, et al. (27) have shown with mice that when the energy disposition occurs within a closed, filled cavity such as the skull, chest, or eye, and when the energy density is great enough to transform the tissue to a vapor or gaseous phase, high pressures will occur at the site of interaction. Because total volume of such a cavity is fixed, resultant transmitted pressures will be attenuated only slightly, and tissue destruction will be produced at sites distant from the original site of radiation. Mendelson and Ackerman (28) however, presented experimental evidence that pressure waves were sharply localized and rapidly attenuated in tissue, and that even Q-switched lasers with peak power of 10^7 watts are not likely to produce damage from shock waves beneath the skin of man.

Ionization effects and X-ray production from laser radiation have not been demonstrated in biological tissues. Igelman et al. (29, 30) failed to inhibit enzymes that are consistently inactivated by ionizing radiation, and Goldman (31) was unable to demonstrate ionization in tissues exposed to Q-switched lasers. Intense pulses capable of producing ionization have been produced by McClung and others (32). Data reported by Derr et al. (33) suggest strongly that free radicals are produced in black mouse skin and fibrinolysin preparations by irradiation with ruby laser output of approximately 100 J. Harmonic generation of other wavelengths in tissues has not been reported.

CRITICAL ORGANS

Eye

The absorption of high-intensity energy in the visible and near-visible portions of the electromagnetic spectrum by the eye has long been known to cause ocular damage (34). The potential ocular hazard of laser radiation was first discussed by Solon, Aronson, and Gould in 1961 (35). For radiation in the visible, near-ultraviolet, and near-infrared regions of the electromagnetic spectrum, the retina is considered the critical part of the eye, whereas in the ultraviolet and infrared regions, the portions of the eye anterior to the retina may be of greater concern. For wavelengths in the near-ultraviolet, visible, and near-infrared regions, the amount of energy required to produce retinal injury is many orders of magnitude less than that required to produce skin damage.

The effectiveness of laser radiation in producing retinal lesions is influenced by several factors: (1) pupil size, (2) spectral transmission through the ocular media, (3) spectral absorption in pigments of the retina and choroid, (4) retinal spot size. The size of the pupil determines how much light may enter the eye. The pupillary diameter varies from approximately 2 to 8 mm with the ambient light level, fixation distance, age, fatigue, and other factors (36, 37). Because the cornea, lens, and other parts of the ocular media have strong absorption bands for wavelengths below about 4,000 Å and above 14,000 Å, only energy in the near-ultraviolet, visible, and near-infrared reach the retina and choroid in amounts sufficient to produce damage, except in unusual cases (38, 39).

Geeraets et al. (40) determined the transmission of light through the human ocular media as a function of wavelength. It extends from approximately 4,000 Å to 14,000 Å exceeding 80% in the range of 5,000 to 9,500 Å. There were two peaks in the near-infrared, a large one at 11,000 Å and a much smaller one (10%) at 13,000 Å. For the ruby wavelength (6,943 Å) more than 94% of the light incident at the corneal surface of the eye coaxial to its principal optical axis will be transmitted to the retina (41). Lens opacities have occurred following irradiation at longer wavelengths in the infrared (42) and the microwave region (43). At frequencies in the ultraviolet, damage to the cornea can result especially at wavelengths shorter than 2,950 Å, to which the cornea is relatively opaque (44).

The radiation which penetrates to the retina encounters three main tissue layers: retina, choroid, and sclera. In each of them, the radiation is subjected in varying degree to reflection, absorption, and transmission. A negligible portion of visible light striking the retina is absorbed by the inner layers of the retina (those first struck by radiation). Absorption of visible light takes place primarily in the melanin granules contained in the outer layer of the retina (pigment epithelium, PE) and in the pigmented cells of the choroid. The degree of pigmentation varies widely among eyes and also among different topographical sites within the eye. Vascularization of the choroid provides an additional source of absorption. Peak absorption in the PE for light incident on the cornea occurs between 5,000 and 5,500 Å, (45).

The first harmonic of neodymium doped glass (5,300 Å) and the green lines in the argon continuous wave (CW) laser are in the spectral region where maximum absorption by the PE occurs. For the ruby wavelength (6,943 Å) about 10% is absorbed in the ocular media of man and, depending on the individual, 15 to 40% is absorbed in the PE and 10 to 80% in the choroid (40, 46). For the neodymium doped glass wavelength (10,600 Å) absorption in the PE varies from 5 to 15%. In this case much of the light is absorbed by the nerve fiber layer of the retina (inner layers), creating the potential hazard of loss of innervation to retinal areas (47). The PE is roughly 10μ thick while the choroid has a thickness of about 100μ. Consequently, the energy absorbed per unit volume (J/cm^3)

in the PE may exceed that absorbed in the choroid by a factor of 10.

The size of the retinal image or spot determines the retinal area which receives the incident radiation. The minimal retinal spot size is limited by diffraction theory to approximately 100μ depending on pupil diameter, wavelength of light, and the degree of spherical aberrations in the eye. Theoretically, the spot size should increase with an increase in wavelength and decrease with increasing pupil diameter. The latter effect is offset by the effect of spherical aberrations which increase with greater pupil diameter. The image size is important in the dissipation of heat. The rate of temperature rise and the time taken to approach a steady state temperature are functions of image size. At very short exposure times, the radial heat flow will be negligible except for very small images. This is supported by histochemical evidence showing minimal radial spread beyond the image diameter for exposure times less than two milliseconds (48). A marked spread of biological damage beyond the confines of the original image was found for longer exposures (>20 ms). Ham et al. (45) plotted the irradiance in W/cm^2 versus image radius in microns for equilibrium temperatures in the retina. The level of irradiance decreased as the image size increased for a given temperature equilibrium.

Threshold Values for Retinal Damage

The threshold values for retinal damage (Table I) may be defined as the energy density required to produce, within a short interval of time (approximately 5 minutes) after exposure, a clinically visible retinal lesion. These values should not be taken as the absolute minimum for retinal damage since injury has been demonstrated at lower levels of irradiance by more refined techniques. Geeraets et al. (48) demonstrated impairment of enzyme activity at levels of irradiance 10 to 15% below those required to produce visible lesions. Also, retinal lesions may not become clinically visible immediately after exposure at low levels of irradiance.

For the rabbit, an energy value of 2.7×10^{-4} J (duration of exposure and size of exposed area was not reported) incident on the eye produced a visible lesion immediately after treatment whereas a lower energy value of 2.1×10^{-4} J produced a lesion detectable 24 to 48 hours after exposure (49). In the rabbit, the faint lesions which represented the threshold values for earlier observations disappeared within 14 days with no residual evidence of atrophy or pigmentation. The energy value necessary to produce a persistent, just detectable lesion 14 days after exposure was 3.4×10^{-4} J entering the eye (49). The anatomical area of the retina that is exposed is also important in establishing a threshold value. Data obtained from the rhesus monkey retina indicated that the macula (most sensitive area of the retina) was approximately two times more sensitive than the paramacular regions (50).

TABLE 1. THRESHOLDS FOR BIOLOGIC DAMAGE BY LASER RADIATION ($\lambda = 6,943 \text{ \AA}$)
AT THE RETINA OF THE EYE

Regulation or Code	Threshold Values		
	Q-Switched (Pulse Duration)	Non-Q-Switched) (Pulse Duration)	Continuous Wave
U. S. Air Force Regulation No. 161-24, Jan. 1967	0.125 J/cm ² (10-100 ns)		
British Ministry of Aviation Code of Practics for Laser Systems	0.07 J/cm ² (30 ns)	0.85 J/cm ² (200 μ s)	
University of California, LRL Hazards Control Quarterly Report 16 and 17, 1964	0.08 J/cm ² (30 ns)	0.7-0.8 J/cm ² (200 μ s)	
Uniform Industrial Hygiene Codes or Regulations for Laser Installations ACGIH - 1968	0.07 J/cm ² (30 ns)	0.85 J/cm ² (200 μ s)	6.0 W/cm ² (white light)

Because of the understandable paucity of information on the human eye, threshold values are based upon data obtained from experimental animals, mostly rabbits. Extrapolation to the human eye must be made with caution. Research on retinal burns and clinical experience have shown that the rabbit retina provides a useful model for estimating a safe level of human exposure (51). The energy values necessary to produce threshold lesions are reported to be significantly lower in the rabbit than in the human (49, 50, 52). To produce a result in the rhesus monkey comparable to that in the rabbit, approximately 50% higher energy levels are required because of differences in pigmentation (50, 52, 53). Very limited results indicate that the human retina is less sensitive than the rhesus retina (50).

Several agencies have published safety standards for laser operations. Thresholds for biologic damage at the retina of the eye used in determining these standards are given in Table I. The threshold values for retinal damage are presented for three separate modes of operation, Q-switched, non-Q-switched, and continuous wave. The distinguishing feature of the Q-switched device is the rate of energy delivery. Power densities ranging from 1 to 100 MW/cm² (even GW/cm²) can be delivered in pulses ranging from about 5 to 100 nanoseconds (ns).

A radiation dose of 0.07 J/cm^2 will produce a visible lesion in the rabbit retina in 30 ns (54). The value is lower by a factor of 10 from that needed to produce a lesion at 200 μs with a non-Q-switched device. The levels are based upon retinal lesions of considerably greater size than the minimal spot size used in safety level calculations; however, it is reasonable to assume that the level is the same for minimal spot sizes for pulse lengths found in most pulsed lasers.

The output for the non-Q-switched devices ranges between the Q-switched and the continuous wave devices. The power output for continuous wave operation of gas lasers and semiconductor diodes rarely exceeds one watt. The hazard to the eye consists primarily of thermal damage to retinal proteins. If it is assumed that the retina of the human eye will tolerate a 1°C temperature rise above normal for considerable periods of time without sustaining irreversible damage, it has been calculated that 10^{-6} watt is a safe power level. Thus, 10^{-6} W incident on a retinal area 10μ in diameter produces a power density of 1.33 W/cm^2 (54). Possible thermal damage to lens proteins should not be overlooked as continued exposure could conceivably lead to opacification.

Maximum Permissible Levels at the Cornea

Some of the codes from the British, University of California, and the American Conference of Government Industrial Hygienists (ACGIH), have also given maximum permissible exposure levels for laser radiation (wavelength 6,943 Å) at the cornea. The establishment of such values would be a realistic approach since the beam intensity would be measured externally in ambient air. The safe irradiance levels at the cornea are determined by calculating the energy density at the cornea which is below that required to produce threshold damage at the retina. The safe corneal irradiance levels vary depending upon wavelength, pupil size, and duration of exposure. The maximum permissible exposure levels for laser radiation (wavelength 6,943 Å) at the cornea as proposed by the ACGIH code are given in Table II. The maximum permissible levels can be adjusted for other wavelengths by considering the amount of energy transmitted to, and absorbed by, the retina. The ACGIH code presents graphs for determining these values.

Skin

Exposure of the skin to laser radiation is an obvious hazard; however, the biological significance is much less than ocular exposure. There is a high probability that persons who work with laser generating equipment receive repeated exposures to their hands. Studies have been conducted on the skin of animals and to a very limited extent on man using a variety of energy levels and wavelengths. Summarizing the results, a certain energy density was required before there was any noticeable effect, either macroscopic or microscopic. The actual energy density required to produce a minimal skin lesion was dependent upon such factors as the degree of pigmentation, thickness of the keratinized surface, presence of hair, and its color.

TABLE 11. MAXIMUM PERMISSIBLE EXPOSURE LEVELS FOR LASER RADIATION AT THE CORNEA FOR DIRECT ILLUMINATION OR SPECULAR REFLECTION AT $\lambda = 6,943 \text{ \AA}$ (ACGIH-1968)

Pupil Size	Q-Switched Pulse (J/cm^2)	Non-Q-Switched Pulse (J/cm^2)	CW Laser (W/cm^2)
Daylight 3-mm pupil	5.0×10^{-8}	5.0×10^{-7}	5.0×10^{-5}
Laboratory 5-mm pupil	2.0×10^{-8}	2.0×10^{-7}	2.0×10^{-5}
Night 7-mm pupil	1.0×10^{-8}	1.0×10^{-7}	1.0×10^{-5}

In swine, epidermal injury could not be detected after exposure of an area 2 mm in diameter to an energy of 2 J (wavelength 6,943 $\text{\AA}$) (14). Injury was apparent with 3 J after an interval of 30 minutes. In the superficial epidermis, the nuclei showed swelling and concentrations of chromatin along with vacuolization. At an energy of 9 J and an image area 2 mm in diameter, subepidermal vesicles formed. At 24 hours and 10 J of energy, the lesion appeared as a vesicle and pustule.

Fine and associates (16) studied the effects of neodymium-doped glass laser radiation (10,600 $\text{\AA}$) on the skin of the Syrian hamster. Exposure to a single pulse (1 ms) of approximately 30 J produced an immediate injury resembling a second degree burn. The gross appearances of the lesions in the skin on the fifth day postirradiation suggested a more severe reaction in the lighter colored areas than in darker regions. This was also reflected in the microscopic appearance, which presented fewer hair follicles in the lighter areas than in the darker areas, coagulation necrosis, and leukocytic infiltration between necrotic areas and viable tissues. Fine et al. (15) studied the internal effects on hamsters following external irradiation of the abdomen with a focused 50 J ruby laser beam. Visceral injury of varying severity was produced and occasionally visceral perforations occurred at later stages.

Goldman (18) observed no changes in the skin of light pigmentation after exposure to low energy laser beams often as high as 5 to 10 J (duration of exposure not reported). The skin of high pigmentation showed significant changes in the epidermis after impact of a low-energy laser, including superficial charring and crusting, and even ulceration. At energy densities above 20 to 25 J a single impact produced epidermal changes in lightly pigmented skin. A single impact up

to 100 J produced significant alterations such as anesthetic areas with changes in the epidermis and modifications in the deeper blood vessels.

In a normal Caucasian volunteer, irradiation of the skin with an unfocused 100 J ruby laser produced an area of instantaneous mild erythema which was insensitive to touch and persisted for four days. Little information is available on the effect of chronic exposure of the skin to laser radiation. In an individual with hypersensitive white skin, chronic exposure over a two-month period to a 0.5 J pulse produced a lesion with atypical cellular changes (55). Attempts to reproduce these changes in other individuals have not been successful.

Several codes give maximum permissible levels for laser radiation of the skin. The British Aviation Ministry code states that the total laser energy incident upon any part of the body other than the eye should not exceed $0.1 \text{ J/cm}^2\text{s}$. The ACGIH Code (Table II) states that the maximum permissible exposure level for the skin should not exceed daylight levels for the eye by a factor of more than 10^6 .

DISCUSSION AND CONCLUSIONS

Concern over the hazards of exposure to laser radiation has resulted in the establishment of guidelines for human exposure by several agencies. Owing to the incompleteness of knowledge concerning biological effects, particularly long-term ones, it is not possible to set firm protection standards at this time. Current guides are based upon the minimum dose required to produce a visible lesion. These threshold values may vary depending upon the criteria by which they are measured. For the eye, threshold damage has been determined by such varying means as ophthalmoscopy, light microscopic histology, histochemical study, and electroretinography. In histochemical studies (48), impairment of enzyme activity was apparent when the energy level of the light beam had been reduced by 10 to 15% below threshold for ophthalmoscopically visible or histologically detectable lesions. This raises the question of how damage in the human might be demonstrated below levels that are clinically apparent.

Very little is known about the potential cumulative effects produced by repeated subthreshold exposures either to the eye or skin. Current data in this area are not sufficient to provide information concerning the possibility of cumulative effects from repeated exposures. There appears to be some conflict over the significance of repeated subthreshold exposures in the production of damage.

Occupational hazards incidental to the use of lasers must be reduced to the very minimum. In addition to beam exposure, other potential hazards include contact with liquid nitrogen or other substances such as coolants, electrical shock, exposures to gases such as ozone, and explosions at capacitor banks, optical pump systems, and target area. A complete safety program is necessary to protect the operating personnel and other persons present at laser installations.

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